Left ventricular septal pacing: Potential application for Cardiac Resynchronization Therapy

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Primary objectives:* To show non-inferiority in acute hemodynamic effect between the best LV septal pacing side and conventional BiV pacing in heart failure patients who are candidates for CRT. Conventional BiV pacing is defined by simultaneously…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON47101

Source
ToetsingOnline

Brief title
Left ventricular septal pacing

Condition

- Heart failures

Synonym
Heart Failure

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Het onderzoek wordt gefinancieerd door de industrie,Medtronic B.V.

Intervention

Keyword: Cardiac Resynchronization Therapy, Left ventricular septum

Outcome measures

Primary outcome

* To show non-inferiority in acute hemodynamic effect (LVdP/dtmax) between the best LV septal pacing side and conventional BiV pacing in heart failure patients who are candidates for CRT.

Secondary outcome

* Comparing the acute hemodynamic effects of the different LV septal pacing sides with RV apical septum pacing, His pacing, RV septum pacing, LV epicardial postero-lateral wall pacing and intrinsic ventricular activation.

* Change in sequence of LV electrical activation during LV septum pacing compared to the above mentioned pacing configurations using electrocardiographic parameters extracted from the VCG or Verathon Heartscape system.

Study description

Background summary

Cardiac pump function depends on physiological electrical activation of the ventricles. This normal activation is disturbed during artificial electrical stimulation (pacing) of the right ventricle (RV), the common therapy to treat symptomatic slow heart rate (*rate control*), as well as during electrical dyssynchrony such as left bundle branch block (LBBB). As a consequence, RV pacing and LBBB reduce cardiac pump function and increase cardiac morbidity and mortality. During the last two decades cardiac resynchronization therapy (CRT) has emerged as treatment to *resynchronize* ventricular electrical activation by pacing the RV and left ventricular (LV) postero-lateral wall almost simultaneously (*biventricular* (BiV) pacing).

Since initial approval of the therapy over 10 years ago, there have been hundreds of thousands of implants worldwide. In the Netherlands currently more than 2000 CRT devices are implanted each year. Large clinical trials have shown that CRT improves LV systolic pump function, reverses structural remodeling, improves quality of life and exercise tolerance, and decrease mortality. However, a significant proportion of apparently suitable patients fail to benefit. Depending on the definition used, the response to CRT is positive in 50-70% of treated patients, leaving 30-50% without significant effect. One of the problems of CRT is proper positioning and fixation of the LV pacing lead in the coronary vein.

Research in our laboratory revealed that in dogs with AV-block and in patients with sinus node disease, pacing at the LV endocardial side of the interventricular septum (LV septal pacing) provides near physiological ventricular activation, near uniform distribution of workload, and near normal pump function. Furthermore, pump function during LV septal pacing was also at least as good as during BiV pacing. A recent study, with acute hemodynamic data in dogs with LBBB and in a small group of patients with LBBB, further indicates that LV septal pacing may be used for CRT, either as single site pacing or in combination with pacing the RV. A weakness of the patient data is that these patients were either non-responders to conventional CRT or patients where no access to the coronary sinus was obtained. Therefore, this group may not be representative for the entire CRT candidate population.

Two factors appear to determine the positive effect of LV septal pacing: the slow impulse conduction across the interventricular septum and the fast impulse conduction along the inner layers of the LV wall through superficial, non-Purkinje fibers. Following this reasoning, we expect that the exact pacing site at the septum is not critical. This would be of great advantage for future applications in patients, since proper implantation of an LV lead in the coronary sinus requires attention in order to position the lead in the latest activated region.

The aim of the present study is to compare the electrophysiological and hemodynamic effects of several modes and sites of LV septal pacing with those of BiV pacing in patients. The results may have a larger impact on future pacing therapy. The LV septum may become an alternative for BiV pacing, but easier to apply, less invasive, and more cost-effective.

Study objective

Primary objectives:
* To show non-inferiority in acute hemodynamic effect between the best LV septal pacing side and conventional BiV pacing in heart failure patients who are candidates for CRT. Conventional BiV pacing is defined by simultaneously pacing the RV apical septum and LV epicardial postero-lateral wall. The acute hemodynamic effect will be assessed by the invasive quantitative LVdP/dtmax

measurement.

Secondary objectives:
* Compare the differences in acute hemodynamic effect between the different LV septal pacing sides and pacing the RV apical septum, His bundle, RV septum, LV epicardial postero-lateral wall, and intrinsic ventricular activation.
* To investigate the effect of LV septal pacing on the sequence of LV electrical activation assessed by 3-dimensional vectorcardiography (VCG) and noninvasive body surface electrocardiographic mapping using the Verathon Heartscape system (developed by Medtronic).

Study design

The present study will investigate the acute hemodynamic effect of LV septal pacing. Thirty consecutive patients who have an indication for CRT according to current international guidelines will be included.

Study measurements: during the study an extra pacemaker lead will be place on either side of the septum (one in the LV and one in the RV). The positions of the pacemaker lead will be varied and during the different locations of the pacemaker leads various measurements will be performed. During each position, the electrical activation of the heart will be measured using a vectorcardiogram and the Verathon Heartscape system. Furthermore, the acute hemodynamic response to CRT is assessed for each pace location using invasive LV dP/dtmax.

Intervention

Extra invasive acute hemodynamic measurements (LVdP/dtmax) measurements will be performed during CRT implantation. The invasive measurements will be used to compare different locations of LV septal pacing with conventional BiV pacing.

Study burden and risks

Invasive acute LVdP/dtmax measurements are performed with a PressureWire, which is inserted via the femoral artery into the LV cavity using the retrograde aortic approach. Using this same entry, the temporary LV pacing electrode or LV steerable EP catheter is placed into the LV cavity. Local vascular complications of femoral artery puncture like bleeding, infection or damage to the vessel wall may occur but are rare. Complication rates have never been published, but will likely not exceed the complication rate of 1.6% observed after diagnostic cardiac catheterization. The LVdP/dtmax measurements by themselves are not harmful for the patient.

The temporary EP catheter used to perform temporary His pacing and RV septum pacing, uses the femoral vein as entry point. Since this entry point is very

close to the femoral artery used for the LV pacing electrode or LV steerable EP catheter and PressureWire (as described above) no additional anaesthetics are needed. Beside a possible haematoma at the inguinal, no other complications are expected. The additional steps taking for the study are His pacing and RV septal pacing. Cardiac complications of pacing the His or the RV with the EP catheter have never been reported and is therefore not considered to carry any risks for the patient.

The placement of the temporary RV septal steerable electrophysiology (EP) catheter, the temporary LV pacing electrode or LV steerable EP catheter and the PressureWire may require a longer fluoroscopy time than usual. During standard CRT implantation patients are exposed to an average radiation dose of 400 mGy. The extra radiation dose will be no more than 25% (100 mGy), which is comparable to the average 1 year background radiation in the Netherlands. Furthermore, the placement of the temporary RV septal steerable EP catheter, the temporary LV pacing electrode or LV steerable EP catheter as well as the intra-procedural measurements with VCG, Verathon Heartscape system, and invasive LVdP/dtmax measurements will increase the total procedure time by a maximum of 1 hour, thus increasing discomfort for the patient. There are no direct benefits for the patient when participating in this study. However, if the current study can validate the use of LV septal pacing in CRT candidates, CRT becomes easier to apply, less invasive, and more cost-effective. Furthermore, LV septal pacing in CRT candidates can also be performed in patients with an inaccessible coronary sinus and/or in patients with phrenic nerve stimulation.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

The study population consists of patients who have an indication for CRT according to current international guidelines. The patients will be recruited from the out-patient pacemaker/ICD clinic and from the cardiology ward.;Inclusion criteria:
* Chronic heart failure with NYHA functional class II-IV
* Left ventricular ejection fraction (LVEF) < 35%
* LBBB and QRS duration * 130 ms or non-LBBB and QRS duration * 150 ms
* In sinus rhythm
* Optimal pharmacological therapy

Exclusion criteria

* Persistent atrial fibrillation
* * 2 premature ventricular complexes on standard 12-lead ECG
* Age < 18 years
* Incapable of giving informed consent
* Moderate to severe aortic valve stenosis
* Peripheral vascular disease

Study design

Design

Study type: Interventional
Masking: Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-10-2017
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO Date:	01-03-2017
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	05-09-2018
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL58809.068.16
Other	Nog niet bekend

Study results

Date completed:	29-04-2019
Actual enrolment:	30